HIV drug resistance surveillance for prioritizing treatment in resource-limited settings

Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The study compared the use of three treatment strategies for human immunodeficiency virus (HIV). The strategies were:

- prophylaxis with co-trimoxazole alone and no antiretroviral treatment (ART);
- ART beginning with a non-nucleoside reverse transcriptase inhibitor (NNRTI)-based regimen followed by a boosted protease inhibitor (PI)-based regimen; and
- ART beginning with a boosted PI-based regimen followed by an NNRTI-based regimen.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis

Study population
The study population comprised a hypothetical cohort of HIV patients with mean CD4 cell count of 331 cells/microL.

Setting
The study setting was secondary care. The economic study was carried out in the USA, France and Cote d'Ivoire.

Dates to which data relate
The effectiveness data were derived from studies published between 1997 and 2005. The price year was 2005.

Modelling
A first-order Monte Carlo state-transmission simulation model of HIV natural history and treatment was applied to resource-limited settings. The model, which had already been published (Yazdanpanah et al. 2005 and Sax et al. 2005, see ‘Other Publications of Related Interest’ for bibliographic details), was developed for a Cote d'Ivoire setting from the US-based Cost-Effectiveness of Preventing AIDS Complications model.

Study designs and other criteria for inclusion in the review
The clinical and epidemiological data used in the economic evaluation were:

- the mean monthly CD4 cell decline due to HIV;
- the monthly risk of severe and mild opportunistic infections (including fungal, bacterial, malaria, tuberculosis, isoporiasis, toxoplasmosis and mycobacteriosis);
- the percentage of patients suppressed at 48 weeks according to sequential ART regimen; and
- the efficacy of co-trimoxazole in reducing severe and mild opportunistic infections.
Sources searched to identify primary studies
Where possible, data derived from the Cote d'Ivoire were used to simulate a representative clinical cohort of chronically infected HIV patients. The incidence of opportunistic infections and their respective mortality were derived from a randomised controlled trial of co-trimoxazole prophylaxis conducted in the Cote d'Ivoire. The effectiveness of alternative ART options was derived from a literature review on ART use in Africa, supplemented with USA data if no information from Africa was available.

Methods used to derive estimates of effectiveness
The authors reported that a review of the literature was undertaken to derive the effectiveness of ART. However, the methods of the review were not reported, i.e. the authors did not report the inclusion criteria or the sources searched to identify relevant studies.

Measure of benefits used in the economic analysis
The measure of benefits used was the life-years gained. Since benefits could be generated over the lifetime of the patient, discounting was relevant and was appropriately performed using an annual rate of 3%.

Direct costs
The direct costs included in the analysis were those of the third-party payer. They included the costs of inpatient care (including length of stay, laboratory tests, clinical procedures and drug dispensed), outpatient care, ART and other medications. Resource use data on the care of HIV patients were derived from the trial used to derive the incidence of opportunistic infections. The costs associated with this resource use were derived from a University Hospital, urban community hospital and from a University Hospital laboratory, all in Abidjan, Cote d'Ivoire. ART costs were taken from negotiated prices for generic fixed-dose combinations for developing countries. Other medication costs were derived from the pharmacy records of Medecins Sans Frontieres and public and private drug suppliers in Cote d'Ivoire. Since the costs could be incurred over the lifetime of the patient, discounting was relevant and was appropriately performed using an annual rate of 3%. The price year was 2005. The authors reported the average costs per patient.

Statistical analysis of costs
The costs were treated as point estimates (i.e. the data were deterministic).

Indirect Costs
Although the authors reported that a societal perspective had been used, productivity costs were not reported.

Currency
US dollars ($). The exchange rate used to convert local currency into US dollars was not reported.

Sensitivity analysis
A series of one- and two-way sensitivity analyses were performed to examine the stability of the model results in the face of alternative assumptions about ART efficacy, drug costs, criteria for starting, stopping and switching ART, and NNRTI resistance.

Estimated benefits used in the economic analysis
The mean discounted life expectancy was:

- 2.78 years with no ART,
- 6.71 years with the boosted PI-based regimen then NNRTI-based regimen, and
- 7.30 years with the NNRTI-based regimen then boosted PI-based regimen.

Cost results
The mean discounted costs were:

- $1,090 with no ART:
$4,970 with the boosted PI-based regimen then NNRTI-based regimen, and

$5,210 with the NNRTI-based regimen then boosted PI-based regimen.

Synthesis of costs and benefits
The authors ranked the three strategies in terms of their costs (from less to more costly) and then calculated incremental cost-effectiveness ratios (ICERs). The authors found that the strategy based on a boosted PI-based regimen followed by an NNRTI-based regimen was dominated by the NNRTI-based regimen followed by a boosted PI-based regimen as, although the former had lower costs per patient, it had a higher cost-effectiveness ratio than the latter and, consequently, its ICER was not reported. When the NNRTI-based regimen followed by a boosted PI-based regimen was compared with no ART, the additional cost per life-year gained was $910.

The results of the sensitivity analyses generally showed that, at lower PI-based regimen costs, starting with a PI-based regimen became cost-effective at lower prevalence of NNRTI resistance (assumed to be 5% in the base-case scenario). In addition, a boosted PI-regimen could have a 48-week HIV RNA suppression rate as low as 26% for the ICER to remain below the cost-effectiveness threshold.

Authors' conclusions
The authors concluded that drug costs and treatment efficacies, not levels of non-nucleoside reverse transcriptase inhibitor (NNRTI), were most influential in determining the optimal HIV drug sequencing in Cote d'Ivoire.

CRD COMMENTARY - Selection of comparators
A justification was given for the comparators used, namely that, in a country similar to Cote d'Ivoire, a total of 10% of the HIV population are primary resistant to NNRTIs. You should decide if the comparators used represent current practice in your own settings.

Validity of estimate of measure of effectiveness
The parameters were derived from published research and, whenever possible, the authors derived clinical and epidemiological data from Cote d'Ivoire settings. The authors reported that a review of the literature was undertaken to derive the effectiveness of ART. However, the methods of the review were not reported, i.e. the authors did not report the inclusion criteria or the sources searched for relevant studies.

Validity of estimate of measure of benefit
The estimation of health benefit (i.e. life-years gained) was derived appropriately using a Monte-Carlo state-transition simulation model. Since the benefits could be generated over the lifetime of the patient, discounting was relevant and was appropriately performed.

Validity of estimate of costs
The authors reported that the study had been conducted from a societal perspective. However, the productivity costs were not included. Therefore, it would appear that the costs were assessed from the perspective of the health care system. All the relevant cost categories and costs for this perspective appear to have been included in the analysis. The omission of productivity losses (i.e. costs of productivity loss due to early death or absence of work through sickness) would appear to have biased the results against the interventions that increased life-expectancy most (i.e. NNRTI-based regimens), as patients had the potential to have worked for a longer time. Resource use and costs were mainly derived from different hospitals in Cote d'Ivoire. Since the costs could be incurred over the lifetime of the patient, discounting was relevant and was appropriately performed. The authors evaluated uncertainty in the model using a series of one-way sensitivity analyses. The price year was reported, which will assist future inflation exercises.

Other issues
The authors did not compare their findings with those from other studies. The issue of the generalisability to other settings was partly addressed in the sensitivity analysis. The authors did not present their results selectively and their conclusions reflected the scope of the analysis. The authors reported a number of limitations to their study. First, the data used to inform the model were derived from numerous sources, some of which were not based in a Cote d'Ivoire NHS Economic Evaluation Database (NHS EED) Produced by the Centre for Reviews and Dissemination Copyright © 2016 University of York
setting. Given the available data for the general population, the efficacy of the NNRTI-based regimen in the setting of nevirapine resistance was derived from women who had previously received nevirapine in order to prevent mother-to-child transmission. Finally, the analysis was restricted to the initial treatment decision.

Implications of the study
The authors reported that the cost-effectiveness of ART sequencing was most influenced by drug costs and efficacy, rather than the prevalence of resistance.

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Other publications of related interest
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MeSH
Anti-HIV Agents /economics /therapeutic use; Antiretroviral Therapy, Highly Active /economics /methods; CD4 Lymphocyte Count; Cost-Benefit Analysis; Cote d'Ivoire; Decision Making; Drug Costs /statistics & numerical data; Drug Resistance, Viral; HIV Infections /drug therapy /economics /immunology /virology; HIV Protease Inhibitors /economics /therapeutic use; Health Care Rationing /methods; Humans; Models, Biological; Program Evaluation; Reverse Transcriptase Inhibitors /economics /therapeutic use; Sensitivity and Specificity; Sentinel Surveillance; Treatment Outcome

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